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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Application Number	09/394,712
Filing Date	September 13, 1999
First Named Inventor	R. W. ESMOND et al.
Art Unit	1614
Examiner Name	Vickie Y. KIM
Attorney Docket Number	04012.0373-00000

Sheet 1 of 3

U.S. PATENTS AND PUBLISHED U.S. PATENT APPLICATIONS

Examiner Initials	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Issue or Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

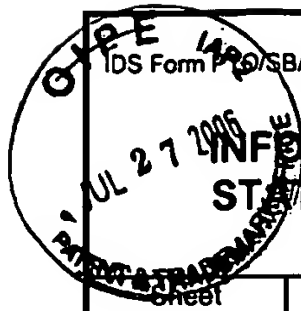
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FOREIGN PATENT DOCUMENTS

Examiner Initials	Cite No. ¹	Foreign Patent Document Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Translation ⁶

NON PATENT LITERATURE DOCUMENTS

Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Translation ⁶
		BEAL et al., "Somatostatin: alterations in the central nervous system in neurological diseases," <i>Res. Publ. Assoc. Res. Nerv. Ment. Dis.</i> , 64: 215-257 (1986).	
		BROE et al., "A case-control study of Alzheimer's disease in Australia," <i>Neurology</i> 40: 1698-1707 (1990).	
		BUCHT et al., "Changes in blood glucose and insulin secretion in patients with senile dementia of Alzheimer type," <i>Acta Med. Scand.</i> , 213: 387-392 (1983).	
		BURGERING et al., "Protein kinase B (c-Akt) in phosphatidylinositol-3-OH kinase signal transduction," <i>Nature</i> , 376: 599-602 (1995).	
		CANTELO et al., "The synthesis of BRL 49653 - a novel and potent antihyperglycaemic agent," <i>Bioorg. Med. Chem. Lett.</i> , 4: 1181-1184 (1994).	
		CARSON et al., "Insulin-like growth factor I increases brain growth and central nervous system myelination in transgenic mice," <i>Neuron</i> , 10: 729-740 (1993).	
		CREWS et al., "Binding of [¹²⁵ I]-insulin-like growth factor-1 (IGF-1) in brains of Alzheimer's and alcoholic patients," <i>Adv. Exp. Med. Biol.</i> , 293: 483-492 (1991).	
		CREWS et al., "Insulin-like growth factor I receptor binding in brains of Alzheimer's and alcoholic patients," <i>J. Neurochem.</i> , 58: 1205-1210 (1992).	
		CURB et al., "The relationship of diabetes and glucose tolerance to Alzheimer's disease and vascular dementia," <i>Neurobiol. Aging</i> , 17(4S): S122 [Abstract 488] (1996).	
		D'ERCOLE et al., "Use of transgenic mice for understanding the physiology of insulin-like growth factors," <i>Horm. Res.</i> , 45 (Supp.1): 5-7 (1996).	
		D'ERCOLE et al., "The role of the Insulin-like growth factors in the central nervous system," <i>Mol. Neurobiol.</i> , 13: 227-255 (1996).	
		De KEYSER et al., "Insulin-like growth factor-I receptor densities in human frontal cortex and white matter during aging, in Alzheimer's disease, and in Huntington's disease," <i>Neurosci. Lett.</i> , 172: 93-96 (1994).	
		de la MONTE et al., "Modulation of neuronal thread protein expression with neuritic sprouting: relevance to Alzheimer's disease," <i>Journal of the Neurological Sciences</i> , 138: 26-35 (1996).	
		de la MONTE et al., "Profiles of neuronal thread protein expression in Alzheimer's disease," <i>Journal of Neuropathology and Experimental Neurology</i> , 55: 1038-1050 (1996).	
		de la MONTE et al., "Characterization of the AD7C-NTP cDNA expression in Alzheimer's disease and measurement of a 41-kD protein in cerebrospinal fluid," <i>J. Clin. Invest.</i> , 100: 3093-3104 (1997).	
		de la MONTE et al., "Neuronal thread protein gene modulation with cerebral infarction," <i>Journal of Cerebral Blood Flow & Metabolism</i> , 17:623-635 (1997).	



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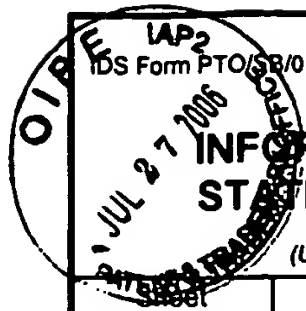
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DUDEK et al., "Regulation of neuronal survival by the serine-threonine protein kinase Akt," <i>Science</i> , 275: 661-665 (1997).	
DUELLI et al., "Intracerebroventricular injection of streptozotocin induces discrete local changes in cerebral glucose utilization in rats," <i>Int. J. Devl. Neuroscience</i> , 12:737-743 (1994).	
FERINI-STRAMBI et al., "Clinical and epidemiological aspects of Alzheimer's disease with presenile onset: a case-control study," <i>Neuroepidemiology</i> , 9: 39-49 (1990).	
FINCH et al., "Aging, metabolism, and Alzheimer disease: Review and hypotheses," <i>Experimental Neurology</i> , 143: 82-102 (1997).	
FISMAN et al., "Metabolic changes in Alzheimer's disease," <i>J. Am. Geriatr. Soc.</i> , 36: 298-300 (1988).	
FOLLI et al., "The early intracellular signaling pathway for the insulin/insulin-like growth factor receptor family in the mammalian central nervous system," <i>Mol. Neurobiol.</i> , 13: 155-183 (1996).	
FUJISAWA et al., "Increased insulin levels after OGTT load in peripheral blood and cerebrospinal fluid of patients with dementia of Alzheimer type," <i>Biol. Psychiatry</i> , 30: 1219-1228 (1991).	
GARVER et al., "Tau phosphorylation in brain slices: pharmacological evidence for convergent effects of protein phosphatases on tau and mitogen-activated protein kinase," <i>Mol. Pharmacol.</i> , 47: 745-756 (1995).	
GLENNER et al., "Alzheimer's disease: initial report of the purification and characterization of a novel cerebrovascular amyloid protein," <i>Biochem. Biophys. Res. Commun.</i> , 120: 885-890 (1984).	
GOTTFRIES, "Therapy options in Alzheimers-Disease," <i>Brit. J. Clin. Practice</i> , 48(6):327-330 (1994).	
HEIDENREICH et al., "Insulin receptors mediate growth effects in cultured fetal neurons. I. Rapid stimulation of protein synthesis," <i>Endocrinology</i> , 125: 1451-1457 (1989).	
HEYMAN et al., "Alzheimer's disease: A study of epidemiological aspects," <i>Ann. Neurol.</i> , 15: 335-341 (1984).	
HIRSCH et al., "Mitochondrial permeability transition in apoptosis and necrosis," <i>Cell Biol. Toxicol.</i> , 14: 141-145 (1998).	
HOYER et al., "Predominant abnormality in cerebral glucose utilization in late-onset dementia of the Alzheimer type: a cross-sectional comparison against advanced late-onset and incipient early-onset cases," <i>J. Neural Transm. [P-D Sect]</i> , 3: 1-14 (1991).	
HOYER et al., "Cerebral excess release of neurotransmitter amino acids subsequent to reduced cerebral glucose metabolism in early-onset dementia of Alzheimer type," <i>J. Neural Transm.</i> , 75: 227-232 (1989).	
HOYER, "Somatostatin and Alzheimer's disease," <i>J. Neurol.</i> , 234: 266-267 (1987).	
HOYER, "Age as risk factor for sporadic dementia of the Alzheimer type?," <i>Ann. NY Acad. Sci.</i> , 719: 248-256 (1994).	
HOYER, "Neurodegeneration, Alzheimer's disease, and beta-amyloid toxicity," <i>Life Sci.</i> , 55: 1977-1983 (1994).	
KOKMEN et al., "Clinical risk factors for Alzheimer's disease: a population-based case-control study," <i>Neurology</i> , 41:1393-1397 (1991).	
KULIK et al., "Antiapoptotic signalling by the insulin-like growth factor I receptor, phosphatidylinositol 3-kinase, and Akt," <i>Mol. Cell. Biol.</i> , 17: 1595-1606 (1997).	
LAM et al., "The phosphatidylinositol 3-kinase serine kinase phosphorylates IRS-1. Stimulation by insulin and inhibition by Wortmannin," <i>J. Biol. Chem.</i> , 269: 20648-20652 (1994).	
LANDIN et al., "Low blood pressure and blood glucose levels in Alzheimer's disease evidence for a hypometabolic disorder?" <i>J. Intern. Med.</i> , 233: 357-363 (1993).	
LEIBSON et al., "Risk of dementia among persons with diabetes mellitus: a population-based cohort study," <i>Am. J. Epidemiol.</i> , 145:301-308 (1997).	
LORENZO et al., "Amyloid fibril toxicity in Alzheimer's disease and diabetes," <i>Ann. NY Acad. Sci.</i> , 777: 89-95 (1996).	
LOVESTONE et al., "Alzheimer's disease-like phosphorylation of the microtubule-associated protein tau by glycogen synthase kinase-3 in transfected mammalian cells," <i>Curr. Biol.</i> , 4: 1077-1086 (1994).	
MANDELKOW et al., "Tau protein and Alzheimer's disease," <i>Neurobiology of Aging</i> , 15(2):S85-S86 (1994).	
McDERMOTT et al., "Degradation of Alzheimer's β -amyloid protein by human and rat brain peptidases: involvement of insulin-degrading enzyme," <i>Neurochem Res.</i> , 22: 49-56 (1997).	
MENEILLY et al., "Alterations in glucose metabolism in patients with Alzheimer's disease," <i>J. Am. Geriatr. Soc.</i> , 41: 710-714 (1993).	
MESSIER et al., "Glucose regulation and cognitive functions: relation to Alzheimer's disease and diabetes," <i>Behav. Brain Res.</i> , 75: 1-11 (1996).	
MILL et al., "Insulin, insulin-like growth factor II, and nerve growth factor effects on tubulin mRNA levels and	



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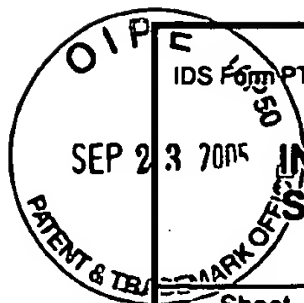
NON PATENT LITERATURE DOCUMENTS

	neurite formation," <i>Proc. Natl. Acad. Sci. USA</i> , 82: 7126-7130 (1985).	
	MOROO et al., "Loss of insulin receptor immunoreactivity from the substantia nigra pars compacta neurons in Parkinson's disease," <i>Acta Neuropathol.</i> , 87: 343-348 (1994).	
	MORTEL et al., "Analysis of familial and individual risk factors among patients with ischemic vascular dementia and Alzheimer's disease," <i>Angiology</i> , 44: 599-605 (1993).	
	NIELSON et al., "Apolipoprotein-E genotyping of diabetic dementia patients: Is diabetes rare in Alzheimer's disease," <i>J. Am. Geriatr. Soc.</i> , 44: 897-904 (1996).	
	NILLNI et al., "Identification of the thyrotropin-releasing hormone precursor, its processing products, and its coexpression with convertase 1 in primary cultures of hypothalamic neurons: anatomic distribution of PC1 and PC2," <i>Endocrinology</i> , 137: 5651-5661 (1996).	
	NISHIYAMA et al., "Expression of the gene encoding the tyrosine kinase-deficient human insulin receptor in transgenic mice," <i>Gene</i> , 141: 187-192 (1994).	
	O'HARE et al., "Intrinsic kinase activity of the insulin receptor," <i>Int. J. Biochem.</i> , 22: 315-324 (1990).	
	OTT et al., "Association of diabetes mellitus and dementia: the Rotterdam Study," <i>Diabetologia</i> , 39: 1392-1397 (1996).	
	PLASCHKE et al., "Action of the diabetogenic drug streptozotocin on glycolytic and glycogenolytic metabolism in adult rat brain cortex and hippocampus," <i>Int. J. Dev. Neurosci.</i> , 11: 477-483 (1993).	
	PURO et al., "Insulin-mediated regulation of neuronal maturation," <i>Science</i> , 225: 1170-1172 (1984).	
	REUBI et al., "Somatostatin and Alzheimer's disease: a hypothesis," <i>J. Neurol.</i> , 233: 370-372 (1986).	
	SPINDLER et al., "Nutritional status of patients with Alzheimer's disease: a 1-year study," <i>J. Am. Diet Assoc.</i> , 96: 1013-1018 (1996).	
	SUN et al., "Structure of the insulin receptor substrate IRS-1 defines a unique signal transduction protein," <i>Nature</i> , 352: 73-77 (1991).	
	SUN et al., "Pleiotropic insulin signals are engaged by multisite phosphorylation of IRS-1," <i>Mol. Cell. Biol.</i> , 13: 7418-7428 (1993).	
	THAM et al., "Insulin-like growth factors and somatomedin B in the cerebrospinal fluid of patients with dementia of the Alzheimer type," <i>Acta Psychiatr. Scand.</i> , 77: 719-723 (1988).	
	THAM et al., "Insulin-like growth factors and insulin-like growth factor binding proteins in cerebrospinal fluid and serum of patients with dementia of the Alzheimer type," <i>J. Neural Transm. [P-D Sect.]</i> , 5: 165-176 (1993).	
	THORPE et al., "Comorbidity of the other chronic age-dependent diseases in dementia," <i>Aging Clin. Exp. Res.</i> , 6: 159-166 (1994).	
	ULLRICH et al., "Human insulin receptor and its relationship to the tyrosine kinase family of oncogenes," <i>Nature</i> , 313: 756-761 (1985).	
	UNGER et al., "Insulin receptors in the central nervous system: localization, signalling mechanisms and functional aspects," <i>Prog. Neurobiol.</i> , 36: 343-362 (1991).	
	UNGER et al., "Immunohistochemical localization of insulin receptors and phosphotyrosine in the brainstem of the adult rat," <i>Neuroscience</i> , 42: 853-861 (1991).	
	WHITE et al., "Insulin rapidly stimulates tyrosine phosphorylation of a Mr-185,000 protein in intact cells," <i>Nature</i> , 318: 183-186 (1985).	
	WINOGRAD et al., "Blood glucose and insulin response in patients with senile dementia of the Alzheimer's type," <i>Biol. Psychiatry</i> , 30: 507-511 (1991).	
	WOLF-KLEIN et al., "Are Alzheimer patients healthier?" <i>J. Am. Geriatr. Soc.</i> , 36: 219-224 (1988).	
	WOZNIAK et al., "The cellular and physiological actions of insulin in the central nervous system," <i>Neurochem. Int.</i> , 22: 1-10 (1993).	
	XU et al., "Ethanol inhibits insulin receptor substrate-1 tyrosine phosphorylation and insulin-stimulated neuronal thread protein gene expression," <i>Biochem. J.</i> , 310: 125-132 (1995).	
	YE et al., "In vivo actions of insulin-like growth factor-I (IGF-I) on cerebellum development in transgenic mice: evidence that IGF-I increases proliferation of granule cell progenitors," <i>Dev. Brain Res.</i> , 95: 44-54 (1996).	

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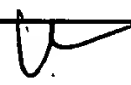
U.S. PATENTS AND PUBLISHED U.S. PATENT APPLICATIONS

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		Roses, Allen D., patent application filed on September 22, 2005, at the U.S. Patent and Trademark Office for "Novel Method."	

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